REMARKS

Rejections of Claims and Traversal Thereof

In the December 28, 2005 Office Action, the rejection was maintained of claims 1-3, 6-11, 13-16, 24 and 73-79 under U.S.C. §112, first paragraph as failing to comply with the written description requirement. This rejection is hereby traversed because there is no infirmity in the presently claimed invention under §112, first paragraph, written description requirements.

Claim 1, as amended herein, is representative of applicants' claimed invention and recites as follows:

> 1. A chimeric polypeptide comprising: a virus coat polypeptide sequence, a viral cell surface receptor polypeptide and an amino acid sequence spacer, wherein the amino acid sequence of the chimeric polypeptide is a full length reference sequence, a truncated sequence or a modified sequence, wherein the modified sequence has about 95% identity to the full length reference sequence or truncated sequence, and wherein the chimeric polypeptide has the functionality of forming an intramolecular interacting complex between the virus coat polypeptide and viral cell surface receptor **and interacting with or blocking a cellular co-receptor that is utilized by a virus for infection**, wherein the virus is an immunodeficiency virus selected from the group consisting of retroviruses HIV, SIV, FIV, and FeLV, wherein the viral cell surface receptor polypeptide sequence comprises amino acid residues of the region of CD4 having binding-affinity for the virus coat polypeptide sequence, and the amino acid sequence spacer is linked to both the virus coat polypeptide sequence and the viral cell surface receptor polypeptide sequence and positioned therebetween to form a single chain polypeptide of peptidic bonds, wherein the spacer consists of an amino acid sequence of sufficient length to allow the single chain polypeptide to fold thereby permitting the virus coat polypeptide sequence and the viral cell surface receptor polypeptide sequence to form the intramolecular interacting complex. (emphasis added)

Applicants' invention is directed to a chimeric polypeptide that comprises polypeptides from a ligand-receptor pair that have a binding affinity for each other and are capable of interacting with a co-receptor to reduce virus access to the co-receptor.

Compliance with §112 requires sufficient information in the specification to show that the applicants possessed the invention at the time of the original disclosure. Applicants' specification meets this requirement because the specification provides ample proof that applicants fully possessed the invention at the time of filing. Further, applicants have included in the specification ample disclosure of the structures of the chimeric polypeptides and their related functionality. Specifically, applicants have included extensive experimental data to meet the written description requirement by identifying characteristics and properties of the chimeric polypeptides of the present invention.

The specification discloses chimeric polypeptides that include virus coat polypeptides and surface cell receptor polypeptides. The receptor and coat polypeptides can be of any amino acid length but of a sufficient length to allow the formation of an intramolecular complex between the receptor and coat polypeptides. The applicable receptor and coat polypeptide sequences include native full-length receptor and full-length coat polypeptide sequences as well as parts of the polypeptide sequences. For example, amino acid truncations, internal deletions or subunits of receptor and coat polypeptide sequences are included.

The specification provides multiple examples showing the structural and related functionality of the claimed chimeric single chain polypeptides. For instance, Example I describes the synthesis of full length and truncated chimeric polypeptides. Example III shows that both the full length and truncated chimeric polypeptide have the ability to form intramolecular complexes and the formed intramolecular complexes cause exposure of a co-receptor binding domain, as described on page 44 of the specification. Importantly, the formation of an intramolecular complex allows for co-receptor binding sites that can be verified by the binding of known antibodies specific for these exposed co-receptor binding sites. As such, the functionality of the chimeric polypeptides of the present invention, including formation of intramolecular complex and co-receptor binding, can be easily verified. As shown in Figures 5 A and B, the antibodies 17b and 48d, that are known to bind within the co-receptor attachment site induced by CD4 binding, reacted strongly with both the full length single chain and truncated single chain chimeric polypeptides of the present invention. These results show that single chain chimeric polypeptides of the present invention are properly folded and form interacting complexes similar to transition state HIV-CD4 complexes.

Example IV describes the data demonstrating the binding of gp120-CD4 chimeric molecules, containing a CCR5-specific HIV envelope sequence, to CCR5 expressing cells. **Interestingly the results shown in this example demonstrate the binding affinity of gp120 with CD4 whether in full length or truncated form.**

Another measure of properly folded gp120-CD4 complexes and its ability to inhibit virus infection of a cell is the ability to bind to a CCR5 co-receptor. Example V, at page 48 of the application, describes data demonstrating that a gp120-CD4 chimeric molecule can neutralize infection by HIV strains using the same co-receptor. As shown in FIG. 8, both FLSC and TcSC potently and selectively neutralized the R5 HIV-1 BaL isolate, while there was only a slight inhibition (ID_{90} > 10 ug/ml) of 2044 isolate. **Thus, the data demonstrate that a virus coat polypeptide-receptor chimeric molecule can bind to a cellular co-receptor thereby blocking binding or infection of the cells by virus that utilize the co-receptor for binding or infection.**

Example VI further describes the construction and expression of a modified gp120-CD4 chimeric polypeptide having an immunoglobulin polypeptide sequence, gp120-CD4-IgG1. This exemplary heterologous domain adds functionality to the gp120-CD4 chimeric polypeptide, including adhesin and immunopotentiating functions, prolonging stability, increasing circulating half-life and ability to cross the placental barrier. This example also shows that the gp120-CD4-IgG1 chimera binds to co-receptor expressed on the surface of intact cells and neutralizes HIV virus. This interaction permits the infection of HIV-1 into target CD4+ cells.

Instructions are provided in the specification for preparing and determining the activity of the chimeras having an additional heterologous domain. As shown in FIG. 11, gp120-CD4-IgG1 binds specifically to L 1.2 cells that express CCR5. These studies indicate that heterologous domains conferring additional or enhanced functionality can be added to chimeric molecules without affecting their ability to form a complex that binds to cell co-receptor.

Further applicants showed that the chimeric polypeptide gp120-CD4-IgG1 of the present invention was just as effective as known antibodies in blocking virus entry into cells, as shown in Table 2 of the application. Thus, one skilled in the art would have no difficulty in discerning that applicants were in possession of all aspects of the claimed invention at the time of filing.

In light of the guidance provided by example 14 in the training material entitled "SYNOPSIS OF APPLICATION OF WRITTEN DESCRIPTION GUIDELINES," applicants insist that the presently claimed invention fully meets the written description requirements.

For example, a review of the full content of the specification indicates that the chimeric polypeptides includes sequences for a virus coat polypeptide and cell surface receptor having amino acid sequences known to the skilled artisan. The chimeric polypeptides of the present invention are novel and unobvious and have the function of forming an intramolecular interactive binding complex and interacting with or blocking a cellular co-receptor that is utilized by a virus for infection. The procedures for making the variant or modified sequences are conventional and an assay is described in the specification that will identify chimeric variants that have the same functional ability of forming the intramolecular interactive binding complex.

Applicants have described several different chimeric polypeptides including a full length sequence, a modified sequence and a truncated sequence and have shown that these chimeric polypeptides exhibit the functionality defined in the claims. Clearly, these defined chimeric polypeptides are representative of a large group of chimeric polypeptides that exhibit similar functionality and structure. Further, the specification provides an assay for identifying all the structures that are capable of the specified functionality. Clearly, one skilled in the art would conclude that the applicants were in possession of the necessary common attributes possessed by the members of the genus. As such, the disclosure meets the requirements of 35 USC §112, first paragraph as providing adequate description for the scope of the claimed invention.

Thus, applicants submit, in light of the analysis set forth in the PTO guidelines, that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph and provides adequate written description for the claimed invention. Applicants respectfully request the withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Rejoinder of Method Claims

When an application as originally filed discloses a product and the process for making and/or using such product, and only the claims directed to the product are presented for examination,

when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product for examination through rejoinder procedure in accordance with MPEP §821.04, provided that the process claims depend from or include all the limitations of the allowed product claims.

The currently pending method claims include all the limitations of the product claims and meet all standards of enablement, written description and definiteness under 35 U.S.C. §112. Accordingly, the method claims are in form suitable for future examination upon their rejoinder with the allowed product elected claims. Applicants are requesting that all method claims be rejoined, examined and found allowable.

New Power of Attorney and Change of Correspondence Address

Applicant has included herewith an executed Power of Attorney form that revokes the previously filed Power of Attorney and appoints new representation with a new Attorney Docket Number **014835-54.99-002**. Further, applicant requests a Change of Correspondence, so that all communications from the USPTO will be sent to the address associated with Customer Number 24239 and addressed as follows:

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P. O. Box 13706
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Fees Payable

Applicants have included six (6) additional dependent claims resulting in a fee of $300.00. Authorization is hereby given to charge this fee to Deposit Account Number 13-4365 of Moore & Van Allen, PLLC.

Conclusion

Applicants have satisfied all the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Winkler reconsider the patentability of pending claims in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Winkler is requested to contact the undersigned attorney at (919) 286-8089 to resolve same.

Respectfully submitted,

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